

SEQUENCE LISTING

<110> Conklin, Darrell C.
 | Gao, Zeren

<120> MULTI-DOMAIN PROTEINASE INHIBITOR

<130> 00-25

<150> US 60/193,642

<151> 2000-03-31

<160> 13

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 2082

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (376)...(222)

<400> 1

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gtgaccctca tggccagtgg ctctgtgctc atgggcctct gggccctccc caacctcctc      60
ccctctgccc tgtgtgacc agggcctggg agcccccgca cggttcagac agaggggcca      120
ggctgaagct ggagaggaac cagcgtcaca cagacggcct ctgagaactt ggagaccccg      180
ttaccacccc agcaggggtg tcaggacaag catctgctgc aggcttcagc ctcaggggca      240
aaagggagcc ccggggtcct ggtgggggca ccgaccacag gcccggaggg tggatgcctg      300
caggaagctg ggctctgtgg agcccgagga ggggctggtg gccacacccc ccggccccct      360
ggctcggcgg ccctc atg ccc gcc cta cgt cca ctc ctg ccg ctc ttg ctc      411
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Met Pro Ala Leu Arg Pro Leu Leu Pro Leu Leu Leu

1

5

10

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ctc ctc cgg ctg acc tcg ggg gct ggc ttg ctg cca ggg ctg ggg agc      459
Leu Leu Arg Leu Thr Ser Gly Ala Gly Leu Leu Pro Gly Leu Gly Ser
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15

20

25

| | |
|---|-----|
| cac ccg ggc gtg tgc ccc aac cag ctc agc ccc aac ctg tgg gtg gac | 507 |
| His Pro Gly Val Cys Pro Asn Gln Leu Ser Pro Asn Leu Trp Val Asp | |
| 30 35 40 | |
| gcc cag agc acc tgt gag cgc gag tgt agc agg gac cag gac tgt gcg | 555 |
| Ala Gln Ser Thr Cys Glu Arg Glu Cys Ser Arg Asp Gln Asp Cys Ala | |
| 45 50 55 60 | |
| gct gct gag aag tgc tgc atc aac gtg tgt gga ctg cac agc tgc gtg | 603 |
| Ala Ala Glu Lys Cys Cys Ile Asn Val Cys Gly Leu His Ser Cys Val | |
| 65 70 75 | |
| gca gca cgc ttc ccc ggc agc cca gct gcg ccg acg aca gcg gcc tcc | 651 |
| Ala Ala Arg Phe Pro Gly Ser Pro Ala Ala Pro Thr Thr Ala Ala Ser | |
| 80 85 90 | |
| tgc gag ggc ttt gtg tgc cca cag cag ggc tcg gac tgc gac atc tgg | 699 |
| Cys Glu Gly Phe Val Cys Pro Gln Gln Gly Ser Asp Cys Asp Ile Trp | |
| 95 100 105 | |
| gac ggg cag ccc gtg tgc cgc tgc cgc gac cgc tgt gag aag gag ccc | 747 |
| Asp Gly Gln Pro Val Cys Arg Cys Arg Asp Arg Cys Glu Lys Glu Pro | |
| 110 115 120 | |
| agc ttc acc tgc gcc tcg gac ggc ctc acc tac tac aac cgc tgc tat | 795 |
| Ser Phe Thr Cys Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr | |
| 125 130 135 140 | |
| atg gac gcc gag gcc tgc ctg cgg ggc ctg cac ctc cac atc gtg ccc | 843 |
| Met Asp Ala Glu Ala Cys Leu Arg Gly Leu His Leu His Ile Val Pro | |
| 145 150 155 | |
| tgc aag cac gtg ctc agc tgg ccg ccc agc agc ccg ggg ccg ccg gag | 891 |
| Cys Lys His Val Leu Ser Trp Pro Pro Ser Ser Pro Gly Pro Pro Glu | |
| 160 165 170 | |
| acc act gcc cgc ccc aca cct ggg gcc gcg ccc gtg cct cct gcc ctg | 939 |
| Thr Thr Ala Arg Pro Thr Pro Gly Ala Ala Pro Val Pro Pro Ala Leu | |
| 175 180 185 | |
| tac agc agc ccc tcc cca cag gcg gtg cag gtt ggg ggt acg gcc agc | 987 |
| Tyr Ser Ser Pro Ser Pro Gln Ala Val Gln Val Gly Gly Thr Ala Ser | |
| 190 195 200 | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| ctc | cac | tgc | gac | gtc | agc | ggc | cgc | ccg | ccg | cct | gct | gtg | acc | tgg | gag | 1035 |
| Leu | His | Cys | Asp | Val | Ser | Gly | Arg | Pro | Pro | Pro | Ala | Val | Thr | Trp | Glu | |
| 205 | | | | | 210 | | | | | 215 | | | | | 220 | |
| aag | cag | agt | cac | cag | cga | gag | aac | ctg | atc | atg | cgc | cct | gat | cag | atg | 1083 |
| Lys | Gln | Ser | His | Gln | Arg | Glu | Asn | Leu | Ile | Met | Arg | Pro | Asp | Gln | Met | |
| | | | | 225 | | | | | 230 | | | | | 235 | | |
| tat | ggc | aac | gtg | gtg | gtc | acc | agc | atc | ggg | cag | ctg | gtg | ctc | tac | aac | 1131 |
| Tyr | Gly | Asn | Val | Val | Val | Thr | Ser | Ile | Gly | Gln | Leu | Val | Leu | Tyr | Asn | |
| | | | 240 | | | | | 245 | | | | | 250 | | | |
| gcg | cgg | ccc | gaa | gac | gcc | ggc | ctg | tac | acc | tgc | acc | gcg | cgc | aac | gct | 1179 |
| Ala | Arg | Pro | Glu | Asp | Ala | Gly | Leu | Tyr | Thr | Cys | Thr | Ala | Arg | Asn | Ala | |
| | | 255 | | | | | 260 | | | | | 265 | | | | |
| gct | ggg | ctg | ctg | cgg | gct | gac | ttc | cca | ctc | tct | gtg | gtc | cag | cga | gag | 1227 |
| Ala | Gly | Leu | Leu | Arg | Ala | Asp | Phe | Pro | Leu | Ser | Val | Val | Gln | Arg | Glu | |
| | 270 | | | | | 275 | | | | | 280 | | | | | |
| ccg | gcc | agg | gac | gca | gcc | ccc | agc | atc | cca | gcc | ccg | gcc | gag | tgc | ctg | 1275 |
| Pro | Ala | Arg | Asp | Ala | Ala | Pro | Ser | Ile | Pro | Ala | Pro | Ala | Glu | Cys | Leu | |
| 285 | | | | | 290 | | | | | 295 | | | | | 300 | |
| ccg | gat | gtg | cag | gcc | tgc | acg | ggc | ccc | act | tcc | cca | cac | ctt | gtc | ctc | 1323 |
| Pro | Asp | Val | Gln | Ala | Cys | Thr | Gly | Pro | Thr | Ser | Pro | His | Leu | Val | Leu | |
| | | | | 305 | | | | | 310 | | | | | 315 | | |
| tgg | cac | tac | gac | ccg | cag | cgg | ggc | ggc | tgc | atg | acc | ttc | ccg | gcc | cgt | 1371 |
| Trp | His | Tyr | Asp | Pro | Gln | Arg | Gly | Gly | Cys | Met | Thr | Phe | Pro | Ala | Arg | |
| | | | 320 | | | | | 325 | | | | | 330 | | | |
| ggc | tgt | gat | ggg | gcg | gcc | cgc | ggc | ttt | gag | acc | tac | gag | gca | tgc | cag | 1419 |
| Gly | Cys | Asp | Gly | Ala | Ala | Arg | Gly | Phe | Glu | Thr | Tyr | Glu | Ala | Cys | Gln | |
| | | 335 | | | | | 340 | | | | | 345 | | | | |
| cag | gcc | tgt | gcc | cgc | ggc | ccc | ggc | gac | gcc | tgc | gtg | ctg | cct | gcc | gtg | 1467 |
| Gln | Ala | Cys | Ala | Arg | Gly | Pro | Gly | Asp | Ala | Cys | Val | Leu | Pro | Ala | Val | |
| | 350 | | | | | 355 | | | | | 360 | | | | | |

| | |
|---|------|
| cag ggc ccc tgc cgg ggc tgg gag ccg cgc tgg gcc tac agc ccg ctg Gln Gly Pro Cys Arg Gly Trp Glu Pro Arg Trp Ala Tyr Ser Pro Leu 365 370 375 380 | 1515 |
| ctg cag cag tgc cat ccc ttc gtg tac ggt ggc tgc gag ggc aac ggc Leu Gln Gln Cys His Pro Phe Val Tyr Gly Gly Cys Glu Gly Asn Gly 385 390 395 | 1563 |
| aac aac ttc cac agc cgc gag agc tgc gag gat gcc tgc ccc gtg ccg Asn Asn Phe His Ser Arg Glu Ser Cys Glu Asp Ala Cys Pro Val Pro 400 405 410 | 1611 |
| cgc aca ccg ccc tgc cgc gcc tgc cgc ctc cgg agc aag ctg gcg ctg Arg Thr Pro Pro Cys Arg Ala Cys Arg Leu Arg Ser Lys Leu Ala Leu 415 420 425 | 1659 |
| agc ctg tgc cgc agc gac ttc gcc atc gtg ggg cgg ctc acg gag gtg Ser Leu Cys Arg Ser Asp Phe Ala Ile Val Gly Arg Leu Thr Glu Val 430 435 440 | 1707 |
| ctg gag gag ccc gag gcc gcc ggc ggc atc gcc cgc gtg gcg ctc gag Leu Glu Glu Pro Glu Ala Ala Gly Gly Ile Ala Arg Val Ala Leu Glu 445 450 455 460 | 1755 |
| gac gtg ctc aag gat gac aag atg ggc ctc aag ttc ttg ggc acc aag Asp Val Leu Lys Asp Asp Lys Met Gly Leu Lys Phe Leu Gly Thr Lys 465 470 475 | 1803 |
| tac ctg gag gtg acg ctg agt ggc atg gac tgg gcc tgc ccc tgc ccc Tyr Leu Glu Val Thr Leu Ser Gly Met Asp Trp Ala Cys Pro Cys Pro 480 485 490 | 1851 |
| aac atg acg gcg ggc gac ggg ccg ctg gtc atc atg ggt gag gtg cgc Asn Met Thr Ala Gly Asp Gly Pro Leu Val Ile Met Gly Glu Val Arg 495 500 505 | 1899 |
| gat ggc gtg gcc gtg ctg gac gcc ggc agc tac gtc cgc gcc gcc agc Asp Gly Val Ala Val Leu Asp Ala Gly Ser Tyr Val Arg Ala Ala Ser 510 515 520 | 1947 |
| gag aag cgc gtc aag aag atc ttg gag ctg ctg gag aag cag gcc tgc Glu Lys Arg Val Lys Lys Ile Leu Glu Leu Leu Glu Lys Gln Ala Cys 525 530 535 540 | 1995 |

gag ctg ctc aac cgc ttc cag gac tag ccccgagagg ggcctgcgcc 2042
 Glu Leu Leu Asn Arg Phe Gln Asp *

545

accccgctcct ggtgaataaa cgcactccct gtgcctcaga 2082

<210> 2

<211> 548

<212> PRT

<213> Homo sapiens

<400> 2

Met Pro Ala Leu Arg Pro Leu Leu Pro Leu Leu Leu Leu Arg Leu
 1 5 10 15
 Thr Ser Gly Ala Gly Leu Leu Pro Gly Leu Gly Ser His Pro Gly Val
 20 25 30
 Cys Pro Asn Gln Leu Ser Pro Asn Leu Trp Val Asp Ala Gln Ser Thr
 35 40 45
 Cys Glu Arg Glu Cys Ser Arg Asp Gln Asp Cys Ala Ala Ala Glu Lys
 50 55 60
 Cys Cys Ile Asn Val Cys Gly Leu His Ser Cys Val Ala Ala Arg Phe
 65 70 75 80
 Pro Gly Ser Pro Ala Ala Pro Thr Thr Ala Ala Ser Cys Glu Gly Phe
 85 90 95
 Val Cys Pro Gln Gln Gly Ser Asp Cys Asp Ile Trp Asp Gly Gln Pro
 100 105 110
 Val Cys Arg Cys Arg Asp Arg Cys Glu Lys Glu Pro Ser Phe Thr Cys
 115 120 125
 Ala Ser Asp Gly Leu Thr Tyr Tyr Asn Arg Cys Tyr Met Asp Ala Glu
 130 135 140
 Ala Cys Leu Arg Gly Leu His Leu His Ile Val Pro Cys Lys His Val
 145 150 155 160
 Leu Ser Trp Pro Pro Ser Ser Pro Gly Pro Pro Glu Thr Thr Ala Arg
 165 170 175
 Pro Thr Pro Gly Ala Ala Pro Val Pro Pro Ala Leu Tyr Ser Ser Pro
 180 185 190
 Ser Pro Gln Ala Val Gln Val Gly Gly Thr Ala Ser Leu His Cys Asp
 195 200 205
 Val Ser Gly Arg Pro Pro Pro Ala Val Thr Trp Glu Lys Gln Ser His
 210 215 220
 Gln Arg Glu Asn Leu Ile Met Arg Pro Asp Gln Met Tyr Gly Asn Val
 225 230 235 240

Val Val Thr Ser Ile Gly Gln Leu Val Leu Tyr Asn Ala Arg Pro Glu
 245 250 255
 Asp Ala Gly Leu Tyr Thr Cys Thr Ala Arg Asn Ala Ala Gly Leu Leu
 260 265 270
 Arg Ala Asp Phe Pro Leu Ser Val Val Gln Arg Glu Pro Ala Arg Asp
 275 280 285
 Ala Ala Pro Ser Ile Pro Ala Pro Ala Glu Cys Leu Pro Asp Val Gln
 290 295 300
 Ala Cys Thr Gly Pro Thr Ser Pro His Leu Val Leu Trp His Tyr Asp
 305 310 315 320
 Pro Gln Arg Gly Gly Cys Met Thr Phe Pro Ala Arg Gly Cys Asp Gly
 325 330 335
 Ala Ala Arg Gly Phe Glu Thr Tyr Glu Ala Cys Gln Gln Ala Cys Ala
 340 345 350
 Arg Gly Pro Gly Asp Ala Cys Val Leu Pro Ala Val Gln Gly Pro Cys
 355 360 365
 Arg Gly Trp Glu Pro Arg Trp Ala Tyr Ser Pro Leu Leu Gln Gln Cys
 370 375 380
 His Pro Phe Val Tyr Gly Gly Cys Glu Gly Asn Gly Asn Asn Phe His
 385 390 395 400
 Ser Arg Glu Ser Cys Glu Asp Ala Cys Pro Val Pro Arg Thr Pro Pro
 405 410 415
 Cys Arg Ala Cys Arg Leu Arg Ser Lys Leu Ala Leu Ser Leu Cys Arg
 420 425 430
 Ser Asp Phe Ala Ile Val Gly Arg Leu Thr Glu Val Leu Glu Glu Pro
 435 440 445
 Glu Ala Ala Gly Gly Ile Ala Arg Val Ala Leu Glu Asp Val Leu Lys
 450 455 460
 Asp Asp Lys Met Gly Leu Lys Phe Leu Gly Thr Lys Tyr Leu Glu Val
 465 470 475 480
 Thr Leu Ser Gly Met Asp Trp Ala Cys Pro Cys Pro Asn Met Thr Ala
 485 490 495
 Gly Asp Gly Pro Leu Val Ile Met Gly Glu Val Arg Asp Gly Val Ala
 500 505 510
 Val Leu Asp Ala Gly Ser Tyr Val Arg Ala Ala Ser Glu Lys Arg Val
 515 520 525
 Lys Lys Ile Leu Glu Leu Leu Glu Lys Gln Ala Cys Glu Leu Leu Asn
 530 535 540
 Arg Phe Gln Asp
 545

<210> 3

<211> 55

<212> PRT

<213> Homo sapiens

<400> 3

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Thr Asp Ile Cys Lys Leu Pro Lys Asp Glu Gly Thr Cys Arg Asp Phe
 1          5          10          15
Ile Leu Lys Trp Tyr Tyr Asp Pro Asn Thr Lys Ser Cys Ala Arg Phe
          20          25          30
Trp Tyr Gly Gly Cys Gly Gly Asn Glu Asn Lys Phe Gly Ser Gln Lys
          35          40          45
Glu Cys Glu Lys Val Cys Ala
 50          55

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<210> 4

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Glu-Glu tag

<400> 4

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Glu Tyr Met Pro Met Glu
 1          5

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<210> 5

<211> 55

<212> PRT

<213> Artificial Sequence

<220>

<223> peptide motif

<221> VARIANT

<222> (2)...(7)

<223> Xaa = any amino acid

<221> VARIANT

<222> (8)...(9)

<223> Xaa = any amino acid or is not present

<221> VARIANT

<222> (11)...(25)

<223> Xaa = any amino acid

<221> VARIANT

<222> (26)...(29)

<223> Xaa = any amino acid or is not present

<221> VARIANT

<222> (31)...(54)

<223> Xaa = any amino acid

<400> 5

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Cys | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Cys | Xaa | Xaa |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Xaa | Xaa | Xaa | Xaa | Xaa | Cys | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa | Xaa |
| | | 35 | | | | | 40 | | | | | | 45 | | |
| Xaa | Xaa | Cys | Xaa | Xaa | Xaa | Cys | | | | | | | | | |
| | | 50 | | | | 55 | | | | | | | | | |

<210> 6

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> thrombin cleavage site

<400> 6

Leu Val Pro Arg

1

<210> 7

<211> 1644

<212> DNA

<213> Artificial Sequence

<220>

<223> degenerate sequence

<221> misc_feature

<222> (1)...(1644)

<223> n = A,T,C or G

<400> 7

| | | | | | | |
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| atgccngcny | tnmgncnny | nytnccnytn | ytnytnytn | tnmgnytnac | nwsnggngcn | 60 |
| ggnytnytn | cnggnytnng | nwsncayccn | ggngtntgyc | cnaaycaryt | nwsnccnaay | 120 |
| ytntgggtng | aygcncarws | nacntgygar | mgngartgyw | snmgngayca | rgaytgygc | 180 |
| gcngcngara | artgytgyat | haaygtntgy | ggnytncayw | sntgygtngc | ngcnmgntty | 240 |
| ccnggnwsnc | cngcngcncc | nacnacngcn | gcnwsntgyg | arggnttygt | ntgyccncar | 300 |
| carggnwsng | aytgygayat | htgggayggn | carccngtnt | gymgntgymg | ngaymgntgy | 360 |
| garaargarc | cnwsnttyac | ntgygcnwsn | gayggnytna | cntaytayaa | ymgntgytay | 420 |
| atggaygcng | argcntgyyt | nmgnggnytn | cayytncaya | thgtncntg | yaarcaygt | 480 |
| ytnwsntggc | cncnwsnws | nccnggnccn | ccngaracna | cngcnmgnc | nacnccnggn | 540 |
| gcngcnccng | tnccnccngc | nytnaywsn | wsnccnwsnc | cncargcngt | ncargtnggn | 600 |
| ggnacngcnw | snytncaytg | ygaygtwnsn | ggmngncnc | cncngcngt | nacntgggar | 660 |
| aarcarsnc | aycarmnga | raaytnath | atgmngccng | aycaratgta | yggnaaygt | 720 |
| gtngtnacnw | snathggnc | rytngtnytn | tayaaygcnm | gnccngarga | ycnggnytn | 780 |
| tayacntgya | cngcnmgnaa | ygngcnggn | ytnytnmgng | cngayttycc | nytnwsngtn | 840 |
| gtncarmng | arccngcnmg | ngaygcngcn | ccnwsnathc | cngcnccngc | ngartgyytn | 900 |
| ccngaygtnc | argcntgyac | nggncnccn | wsnccncayy | tngtnytnng | gcaytaygay | 960 |
| ccncarmng | gnggntgyat | gacnttyccn | gcnmngngnt | gygayggngc | ngcnmgnggn | 1020 |
| ttygaracnt | aygargcntg | ycarcargcn | tgygcnmng | gnccnggnga | ycntgygt | 1080 |
| ytnccngcng | tncarggncc | ntgymnggn | tgggarccnm | gntgggcnta | ywsnccnytn | 1140 |
| ytnccarcat | gycayccntt | ygtntayggn | ggntgygarg | gnaayggnaa | yaayttycay | 1200 |
| wsnmngarw | sntgygarga | ygcntgyccn | gtncnmgna | cncnccntg | ymngcntgy | 1260 |
| mgnytnmgw | snaarytngc | nytnwsnytn | tgygnwsng | ayttygcnat | hgtnggnmg | 1320 |
| ytnacngarg | tnytnngarg | rccngargcn | gcnggnggna | thgcnmgngt | ngcnytngar | 1380 |
| gaygtnytna | argaygayaa | ratgggnytn | aarttyytng | gnacnaarta | yytnngargtn | 1440 |
| acnytnwsng | gnatggaytg | ggcntgyccn | tgyccnaaya | tgacngcngg | ngayggncn | 1500 |
| ytnngtnatha | tggngngargt | nmngngayggn | gtngcngtny | tngaygcngg | nwsntaygt | 1560 |
| mgngcngcnw | sngaraarmg | ngtnaaraar | athytngary | tnytngaraa | rcargcntgy | 1620 |
| garytnytna | aymgnttyca | rgay | | | | 1644 |

<210> 8

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> oligonucleotide primer ZC28.995

<400> 8

acttccccac accttgctct ct

22

<210> 9

<211> 21
 <212> DNA
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 <223> oligonucleotide primer ZC28,996

<400> 9
 tgcctcgtag gtctcaaagc c 21

<210> 10
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 <212> DNA
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 <223> oligonucleotide primer ZC29,898

<400> 10
 gtcctctggc actacgaccc gca 23

<210> 11
 <211> 19
 <212> DNA
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 <223> oligonucleotide primer ZC29,899

<400> 11
 acggcaggca gcacgcagg 19

<210> 12
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 <212> DNA
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 <223> oligonucleotide primer ZC37,161

<400> 12
 cctgaccaaa tgtatggcaa cg 22

<210> 13

<211> 23

<212> DNA

<213> Artificial Sequence

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<223> oligonucleotide primer ZC37,160

<400> 13

cctgggtccc tgcctgagt agt

23

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